As indicated above, there is little if any sequence homology shared among the amino termini of Gα subunits. The amino terminal domains of Gα subunits that precede the first β-sheet (containing the sequence motif -LLLLGAGESG- (SEQ ID NO: 2); see Noel et al., *Supra*, for the numbering of the structural elements of Gα subunits) vary in length from 41 amino acids (GPA1) to 31 amino acids (Gαt). Most Gα subunits share the consensus sequence for the addition of myristic acid at their amino termini (MGxxxS-), although not all Gα subunits that contain this motif have myristic acid covalently associated with the glycine at position 2 (Speigel et al., TIES 16: 338-3441, 1991). The role of this post-translational modification has been inferred from studies in which the activity of mutant Gα subunits from which the consensus sequence for myristoylation has been added or deleted has been assayed (Mumby et al., Proc. Nad. Acad. Sci. USA 87: 728-7321990; Linder et al., J. Biol Chem. 266: 4654-4659, 1991; Gallego et al., Proc. Natl. Acad. Sci. USA 89: 9695-9699, 1992). These studies suggest two roles for N-terminal myristoylation. First, the presence of amino-terminal myristic acid has in some cases been shown to be required for association of Gα subunits with the membrane, and second, this modification has been demonstrated to play a role in modulating the association of Gα subunits with Gβγ complexes. The role of myristoylation of the GPA1 gene products is, at present, unknown.

The replacement paragraph presented above incorporates changes as indicated by the marked-up version below.

Some aspects of Gα structure are relevant to the design of modified Gα subunits. The amino terminal 66 residues of GPA1 are aligned with the cognate domains of human Gαs, Gαi2, Gαi3, Gα16 and transducin. In the GPA41Gα hybrids, the amino terminal 41 residues (derived from GPA1) are identical, end with the sequence-LEKQRDKNE-(SEQ ID NO: 1) and are underlined for emphasis. All residues following the glutamate (E) residue at position 41 are contributed by the human Gα subunits, including the consensus nucleotide binding motif -GxGxxG-. Periods in the sequences indicate gaps that have been introduced to maximize alignments in this region. Codon bias is mammalian. For alignments of the entire coding regions of GPA1 with Gαs, Gαi, and Gαo, Gαq and Gαz, see Dietzel and Kurjan (Cell 50: 573, 1987) and Lambright et al. (Nature 369: 621-628, 1994). Additional sequence information is provided by Mattera et al. (FEBS Lett 206: 36-41, 1986), Bray et al. (Proc. Natl. Acad. Sci. USA 83: 8893-8897, 1986) and Bray et al. (Proc. Natl. Acad. Sci. USA 84: 5115-5119, 1987).

As indicated above, there is little if any sequence homology shared among the amino termini of  $G\alpha$  subunits. The amino terminal domains of  $G\alpha$  subunits that precede the first  $\beta$ -sheet (containing the sequence motif-LLLLGAGESG-(SEQ ID NO: 2); see Noel et al., *Supra*, for the numbering of the structural elements of  $G\alpha$  subunits) vary in length from 41 amino acids (GPA1) to 31 amino acids ( $G\alpha$ t).

